REMARKS

Claims 18 and 19 are pending. Claims 1-12, 16, and 17 were withdrawn and are canceled herein without prejudice. Claim 18 has been amended to introduce certain format changes and to more particularly point out what applicants regard as the invention. Support for the amendment is found in the specification, inter alia, at page 7, lines 129. Applicants submit that these amendments raise no issue of new matter. Thus, claims 18 and 19 will remain pending and under examination upon entry of this Amendment.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the March 26, 2004 Final Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

The Claimed Invention

The present invention is based upon applicants' discovery that the chemokine, stromal cell-derived factor 1 ("SDF-1"), is specifically overexpressed in cultured synoviocytes derived from joints affected by rheumatoid arthritis. Thus, blocking the interaction of SDF-1 with its receptor, CXCR4, on peripheral immune cells infiltrating the joint is presented as a novel therapeutic approach for the treatment of rheumatoid arthritis.

Abstract of the Disclosure

The Examiner objected to applicants' amended Abstract under 35 U.S.C. §132 as allegedly containing new matter to the extent that it recited the phrase, "[t]his invention also provides related methods and compositions."

In response, applicants maintain that the Examiner's rejection of the Abstract under 35 U.S.C. §132 is improper. M.P.E.P. §608.01(b), citing 37 C.F.R. 1.72(b). Nevertheless, in order to advance the prosecution of the instant application, applicants have herein amended the Abstract to remove the language objected to by the Examiner. A clean version of the amended abstracted is attached hereto as **Exhibit A.**

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 18 and 19 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

In response to the Examiner's rejection, applicants respectfully traverse and maintain that the specification adequately describes the claimed invention.

The Examiner alleges that the written description is inadequate for claims which encompass the use of SDF-1 and CXCR4 from any mammalian species. In response, applicants note that the instant claims recite the use of a cell, SDF-1, and CXCR4 derived from human or mouse. Accordingly, applicants maintain that claims 18 and 19 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §102(b)

The Examiner rejected claims 18 and 19 under 35 U.S.C. §102(b) as allegedly anticipated by D'Apuzzo et al.

In response to the rejection, applicants respectfully traverse.

The instant claims provide a method for determining whether a non-peptidyl agent inhibits the activation of a CXCR4 receptor by SDF-1, wherein the CXCR4 receptor is expressed by a monocyte cell.

D'Apuzzo teaches the determination of whether an *antibody* induces CXCR4-dependent cell migration in B lymphocytes. D'Apuzzo does *not* teach a method for testing non-peptidyl agents.

In order to anticipate the claimed method, D'Apuzzo must teach each and every element thereof. D'Apuzzo fails this test. Specifically, D'Apuzzo does not teach a method to determine whether a non-peptidyl agent is an inhibitor of SDF-1 induced activation CXCR4 using monocyte cells. Thus, D'Apuzzo fails to anticipate the claimed invention. Accordingly, applicants maintain that claims 18 and 19 satisfy the requirements of 35 U.S.C. §102(b).

Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants request that the following disclosures be made of record in the above-identified application pursuant to 37 C.F.R. §1.97(b). These references are also listed on the Form PTO-1449 attached hereto as **Exhibit B**. Items 1-20 are attached hereto as **Exhibits 1-20**, respectively.

1. U.S. Serial No. 5,563,048, Honjo et al., issued October 8, 1996;

2. U.S. Serial No. 5,021,409, Murrer et al., issued June 4, 1991;

3. Bleul C.C. et al., A Highly Efficacious Lymphocyte Chemoattractant, Stromal Cell-Derived Factor 1 (SDF-1), J. Exp. Med. (1996) 184:1101-9;

4. Bombara, M.P. et al., Cell Contact Between T Cells and Synovial Fibroblasts Causes Induction of Adhesion Molecules and Cytokines, J. Leukoc. Biol. (1993) 54(5):399-406;

5. Datema, R. et al., Antiviral Efficacy in vivo of the Anti-Human Immunodeficiency Virus Bicyclam SDZ SID 791 (JM 3100), an Inhibitor of Infectious Cell Entry, Antimicrob. Agents and Chemo. (1996) 40:750-754;

6. De Vreese, K. et al., The Bicyclams, a New Class of Potent Human Immunodeficiency Virus Inhibitors, Block Viral Entry after Binding, Antiviral Res. (1996) 29:209-19;

7. Delgado, E., et al., Mature Dendritic Cells Respond to SDF-1, but Not to Several Beta Chemokines, Immunobiology (1998) 198:490-500;

8. Dinant, H.J. and Dijkmans, B.A., New Therapeutic Targets for Rheumatoid Arthritis, Pharm. World. Sci. (April 1999);

9. D'Apuzzo M. et al., The Chemokine SDF-1, Stromal Cell-Derived Factor 1, Attracts Early Stage B Cell

Precursors via the Chemokine Receptor CXCR4, Eur. J. Immunol. (1997) 27:1788-1793;

10. Goddard D.H. et al., Autocrine Regulation of Rheumatoid Arthritis Synovial Cell Growth in vitro, Cytokine (1990) 2:149-155;

11. Iacobelli S. et al., Detection of Antigen Recognized by a Novel Monoclonal Antibody in Tissue and Serum from Patients with Breast Cancer, Cancer Res. (1986) 46(6):3005-3010;

12. Nagasawa T., et al., Defects of B-Cell Lymphopoiesis and Bone-Marrow Myelopoiesis in Mice Lacking the CXC Chemokine PBSF/SDF-1, Nature (1996) 382:635-8;

13. Ponteziere C., et al., Comparative Proliferation of Non-Rheumatoid Human Synovial Cells, Int. J. Tissue React. (1990) 12(4):229-236;

14. Ritchlin C.T. et al., Sustained and Distinctive Patterns of Gene Activation in Synovial Fibroblasts and Whole Synovial Tissue Obtained from Inflammatory Synovitis, Scand. J. Immunol. (1994) 40(3):292-9;

15. Ritchlin C.T. and Winchester R.J., Potential Mechanisms for Coordinate Gene Activation in the Rheumatoid Synoviocyte: Implications and Hypotheses, Springer Semin. Immunopathol. (1989) 11:219-234;

16. Schols et al., Bicyclams, A Class of Potent Anti-HIV Agents, Are Targeted at the HIV Coreceptor Fusin/CXCR-4, Antiviral Research (1997) 35:147-156;

17. Shirozu M. et al., Structure and Chromosomal Loacalization of the Human Stromal Cell-Derived Factor 1 (SDF-1) Gene, Genomics (1995) 28(3):495-500;

18. Smith C.A., Properties of Synovial Cells in Culture, J. Exp. Med. (1971) 134(3):306s-312s;

19. Winchester, R. et al., Alteration of Synoviocytes by Inflamation - The Source of a Persistent Non-Immunologic Drive in Synovitis: Analysis of Levels of mRNA Expression by a Simple Multi-Gene Assay, Clin. Exp. Rheumatol. (1993) 11 Suppl 8:S87-90; and

20. Zou, Y.R. et al., Function of the Chemokine Receptor CXCR4 in Haematopoiesis and in Cerebellar Development, Nature (1998) 393:595-9.

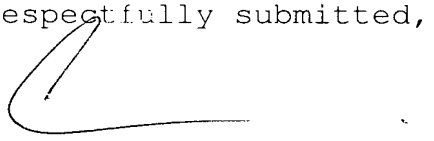
Summary

In view of the remarks made herein, applicants maintain that the claim pending in this application is in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the RCE filing fee, is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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5/20/07
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EXHIBIT A

Abstract of the Disclosure

This invention provides a method for treating rheumatoid arthritis and other forms of inflammatory arthritis which comprises administering to a subject an amount of an agent effective to inhibit the activation of the CXCR4 receptor by SDF-1.